REMARKS

Claims 1-53 are rejected. Claim 54 is withdrawn from consideration. Claims 1, 7, 9, 13, 25, 28, 33, 42 and 54 have been amended. Claims 5, 6 and 34 have been canceled. New Claim 55, depending from claim 27 of Group I has been added. Claims 1-4, 7-33, 35-53 and 55 are presently pending in the application. Favorable reconsideration of the application in view of the following remarks is respectfully requested.

The basis for the amendment of Claim 1 is found in Claims 5, 6 and 34 as originally filed. The basis of new claim 55 is found in claim 28 as originally filed.

Restriction under 35 USC § 121:

The Examiner has required restriction to one of the following inventions under 35 U.S.C. § 121: Group I. Claims 1-53, drawn to a microarray, classified in class 435, subclass 287.8, for example, or Group II. Claim 54, drawn to method of using a microarray, classified in class 435, subclass 4, indicating that the inventions are distinct, each from the other because the inventions I and II are related as product and process of use and either the process for using the product as claimed can be practiced with another materially different product or the product as claimed can be used in a materially different process of using that product or both. In the instant case, the Examiner indicates that the product as claimed can be used in a materially different process, since, for example, the microarray of Group I can be used to detect biological targets using non-optical detection methods such as electrochemical methods.

The Applicants traverse the restriction requirement. As stated by the Examiner, Claim 1 is limited to a microarray, and Claim 54 is drawn to a method of using a microarray. The independent claims claim a microarray comprising a support having attached to a surface thereof at least one porous layer, wherein said porous layer comprises a hydrophilic binder and polymer particles, wherein the polymer particles are monodisperse polymer particles having a particle size distribution coefficient of variation of less than 20% and a mean diameter of from 0.05 to 50 microns. Therefore, it is suggested that commonality exists among the Groups identified by the Examiner with respect to a microarray with a surface porous layer of hydrophilic binder and polymer particles, which have a particle size distribution coefficient of variation of less

than 20% and a mean diameter of from 0.05 to 50 microns. Coextensive searching of the two Groups would not prove seriously burdensome to the Examiner, but would instead be most efficient. In the instant case, the Examiner indicates that the product as claimed can be used in a materially different process, since, for example, the microarray of Group I can be used to detect biological targets using non-optical detection methods such as electrochemical methods. However, claim 54 does not limit "measuring" to optical methodology. Therefore, it is respectfully requested that the Restriction Requirement be reconsidered and withdrawn and that all claims now pending be examined.

Applicants confirm the telephone conversation on May 23, 2005 in which a provisional election was made without traverse to prosecute the invention of Group I, claims 1-53.

Specification:

The Examiner has requested amendment of the specification to capitalize trademarks, to be accompanied by the generic terminology. The specification has been amended accordingly.

Regarding the trademarks FC-10® (p16, line 9), FC-171R® (p16, line 9), DC 1248® (p16, line 13), DC200®(p16, line 13), DC510® (p16, line 13), DC 190® (p16, line 13), BYK 320® (p16, line 14), BYK 322® (p16, line 14), SF 1079® (p16, line 14), SF 1023® (p16, line 14), SF 1054® (p16, line 14), and SF 1080® (p16, line 15), the Applicant is unclear how to modify these marks, as they are already capitalized with the accompanying symbol for trademarks. The Applicant was unable to find FC-439® (p16, line 9), and FC-341® (p16, line 9).

Rejection of Claims 9, 13, 28 and 33 under 35 U.S.C. § 112:

The Examiner has rejected Claims 9, 13, 28 and 33 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, as Claim 9 recites the limitation "said specific functionalities" without sufficient antecedent basis for this limitation in the claim, Claim 13 recites the limitation "said specific functionalities" without sufficient antecedent basis for this limitation in the claim, and, regarding claims 28 and 33, the phrase "such as" renders the claim indefinite.

Claims 9, 13, 28, and 33 have been amended accordingly.

Rejection of Claims 1-4, 8-11, 43, 44, 45 and 47-52 Under 35 U.S.C. §102(b):

The Examiner has rejected Claims 1-4, 8-11, 43, 44, 45 and 47-52 under 35 U.S.C. §102(b) as being anticipated by Wohlstadter et al. (U.S. Patent No. 6,066,448), which teaches a microarray comprising a support having attached to a surface thereof at least one porous layer, wherein the porous layer comprises a hydrophilic binder and polymer particles.

Wohlstadter discloses materials and methods for producing patterned multi- array, multi-specific surfaces that are electronically excited for use in electrochemiluminescence based tests. Materials and methods are provided for the chemical and/or physical control of conducting domains and reagent deposition for use in flat panel displays and multiply specific testing procedures.

The present invention relates to a microarray comprising a support having attached to a surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles, which have a particle size distribution coefficient of variation of less than 20% and a mean diameter of from 0.05 to 50 microns.

A claim is anticipated only if each and every element as set forth in the claim is found either expressly or inherently described in a single prior art reference. Original claim 1 has been amended to include previously dependent claims 5, 6, and 34. Wohlstadter fails to disclose monodisperse polymer particles with the required coefficient of variation of less than 20% and a mean diameter of 0.05 to 50 microns. Therefore, Wohlstadter does not set forth each and every element as set forth in the claims of the present invention and does not expressly or inherently describe in as complete detail as is contained in the claims of the present invention the limitations and requirements of the present invention. Therefore the reference does not anticipate the present invention. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C §102(b).

Rejection of Claims 5, 13, 16-24, 36-42, 46 and 53 Under 35 U.S.C. §103(a):

The Examiner has rejected Claims 5, 13, 16-24, 36-42, 46 and 53 under 35 U.S.C. §103(a) as being unpatentable over Wohlstadter et al. (U.S. Patent No. 6,066,448) in view of Pierce et al. (U.S. Patent No. 4,258,001).

The Examiner indicates that Wohlstadter et al. teaches a microarray as discussed above. The Examiner further indicates that Wohlstadter

et al. fails to teach a microarray, wherein the polymer particles comprise monodisperse polymer particles, stabilizer polymers comprise pendant vinylsulfonyl or latent vinylsulfonyl groups, and hydrophilic binder comprise gelatin.

The Examiner states that Pierce et al. teaches a particulate structure on a support surface containing interactive compositions. The Examiner states that although shape and size of the organo-polymeric particles can vary widely, in a preferred embodiment, these particles are of substantially uniform size (column 9, lines 35-37). The size of the organo-polymeric particles regulate to an extent, the size of the void spaces contained in the particulate structure of the element (column 9, lines 42-44).

The Examiner indicates that it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the microarray of Wohlstadter et al. polymer particles having a substantially uniform size distribution defined as being monodisperse by Pierce et al. (column 30, line 42) in order to readily take up, uniformly distribute within itself, meter, and rapidly transport applied liquid samples containing any of a wide variety of analytes for immunoassays. This rejection is respectfully traversed.

Wohlstadter discloses materials and methods for producing patterned multi- array, multi-specific surfaces that are electronically excited for use in electrochemiluminescence based tests. Materials and methods are provided for the chemical and/or physical control of conducting domains and reagent deposition for use in flat panel displays and multiply specific testing procedures.

Pierce discloses an element for the analysis or transport of liquid, especially aqueous liquids, contains a structure comprising a plurality of heat-stable, organo-polymeric particles non-swellable in and impermeable to the liquid, and an adhesive concentrated at particle surface areas contiguous to adjacent particles bonding the particles into a coherent, three-dimensional lattice that is non-swellable in the liquid. A substantial portion of the particle surface area in this lattice structure is therefore effectively free from adhesive. The lattice structure has interconnected void spaces among the particles representing a total void volume of about 25 to 80 percent to provide for transport of the liquid. The adhesive comprises an organic polymer different from that of the particles and insoluble in the liquid under analysis. The amount of adhesive in the structure is

less than 10 weight percent of the particles. The particulate structure of these elements can contain interactive compositions useful for the analysis of various substances in liquids, especially high molecular weight proteinaceous substances in aqueous biological liquids. Multi-zone elements containing, in fluid contact, at least two zones having a particulate structure as described above or one such zone together with other functional zones are also disclosed. These structures are particularly useful in the "dry chemistry" analysis of aqueous liquids. "Dry chemistry" analysis refers to analytical methods and techniques that are carried out using chemical reagents contained in various "dry-to-the-touch" test elements such as "dip-and-read" test strips, multilayer test elements and the like.

The present invention, as amended relates to a microarray comprising a support having attached to a surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles, which have a particle size distribution coefficient of variation of less than 20% and a mean diameter of from 0.05 to 50 microns.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the references or in the general knowledge available to one skilled in the art to modify the references, there must be a reasonable expectation of success, and the prior art references must teach or suggest all the claim limitations. Original claim 1 has been amended to include previously dependent claims 5, 6, and 34. As noted by the Examiner Wohlstadter fails to teach monodisperse polymer particles. Furthermore, Pierce fails to teach or suggest monodisperse polymer particles with a variation coefficient of less than 20%. The Examiner states that Pierce discloses the use of organo-polymeric particles that are of "substantially uniform size" (column 9, lines 35-37). However, Pierce does not define substantially uniform size as a variation of less than 20% as claimed in the instant invention. In fact, the examples of Pierce (column 34, lines 11-13; column 35, lines 15-16) only show the use of organo-polymeric beads with size variations of greater than 100%. Therefore, it is respectfully urged that Pierce fails to teach or suggest the use of polymer particles with a particle size distribution coefficient of variation of less than 20% as claimed in the instant invention as amended. Wohlstadter and Pierce both fail to teach or suggest monodisperse polymer particles with the required coefficient of variation of less than 20% and a mean diameter of 0.05 to 50 microns as claimed

in the instant invention as amended. Therefore, it is respectfully urged that the combination of these references would not lead one of ordinary skill in the art to the instant invention. Furthermore, claims 6 and 34 as originally filed do not stand rejected under these references, and are now incorporated into independent claim 1. Claims 13, 16-24, 36-42, 46 and 53 benefit from dependency on claim 1, which as discussed above is patentable. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

Rejection of Claims 6 and 7 Under 35 U.S.C. §103(a):

The Examiner has rejected claims 6 and 7 under 35 U.S.C. §103(a) as being unpatentable over Wohlstadter et al. (U.S. Patent No. 6,066,448) in view of Pierce et al. (U.S. Patent No. 4,258,001) as applied to claim 5 above, and further in view of Waki et al. (US 2001/0022769).

The Examiner indicates that Wohlstadter et al. in view of Pierce et al. teaches a microarray as discussed above. The Examiner states that Pierce et al. teaches that although shape and size of the organo-polymeric particles can vary widely, in a preferred embodiment, these particles are of substantially uniform size (column 9, lines 35-37). The Examiner indicates that Wohlstadter et al. in view of Pierce et al. fails to teach a microarray, wherein the monodisperse polymer particles have a particle size distribution with coefficient of the particle size distribution less than 10%.

The Examiner indicates that Waki et al. teaches a method of making monodisperse polymer particles with a narrow particle size distribution. The monodisperse particles have a coefficient of variation of less than 10% column 3, lines 9-11).

The Examiner states that, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the microarray of Wohlstadter et al. in view of Pierce et.al. with a monodisperse polymer particle having coefficient of variation of less than 10% as taught by Waki et al. in order to attain uniform size distribution for particulate structure on a support surface to readily take up, uniformly distribute within itself, meter, rapidly transport applied liquid samples containing any of a wide variety of analytes for immunoassays. This rejection is respectfully traversed.

Wohlstadter discloses materials and methods for producing patterned multi- array, multi-specific surfaces that are electronically excited for

use in electrochemiluminescence based tests. Materials and methods are provided for the chemical and/or physical control of conducting domains and reagent deposition for use in flat panel displays and multiply specific testing procedures.

Pierce discloses an element for the analysis or transport of liquid, especially aqueous liquids, contains a structure comprising a plurality of heat-stable, organo-polymeric particles non-swellable in and impermeable to the liquid, and an adhesive concentrated at particle surface areas contiguous to adjacent particles bonding the particles into a coherent, three-dimensional lattice that is non-swellable in the liquid. A substantial portion of the particle surface area in this lattice structure is therefore effectively free from adhesive. The lattice structure has interconnected void spaces among the particles representing a total void volume of about 25 to 80 percent to provide for transport of the liquid. The adhesive comprises an organic polymer different from that of the particles and insoluble in the liquid under analysis. The amount of adhesive in the structure is less than 10 weight percent of the particles. The particulate structure of these elements can contain interactive compositions useful for the analysis of various substances in liquids, especially high molecular weight proteinaceous substances in aqueous biological liquids. Multi-zone elements containing, in fluid contact, at least two zones having a particulate structure as described above or one such zone together with other functional zones are also disclosed. These structures are particularly useful in the "dry chemistry" analysis of aqueous liquids. "Dry chemistry" analysis refers to analytical methods and techniques that are carried out using chemical reagents contained in various "dry-to-the-touch" test elements such as "dip-and-read" test strips, multilayer test elements and the like.

Waki relates to an optical recording medium, and further to an optical recording method and discloses an optical recording medium comprising a recording layer containing ultra fine particles of a metal having an average particle size of 1 nm to 50 nm, and surfaces thereof being modified with an adsorptive compound.

The present invention relates to a microarray comprising a support having attached to a surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles, which have a particle size distribution coefficient of variation of less than 20% and a mean diameter of from 0.05 to 50 microns.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the references or in the general knowledge available to one skilled in the art to modify the references, there must be a reasonable expectation of success, and the prior art references must teach or suggest all the claim limitations. Original claim 1 has been amended to include previously dependent claims 5, 6, and 34. As noted by the Examiner Wohlstadter fails to teach monodisperse polymer particles. As discussed above, Pierce fails to teach or suggest monodisperse polymer particles with a variation coefficient of less than 20%. As discussed above Wohlstadter and Pierce fail to teach or suggest monodisperse polymer particles with the required coefficient of variation of less than 20% and a mean diameter of 0.05 to 50 microns as claimed in the instant invention as amended. As noted by the Examiner neither Wohlstadter nor Pierce teaches a microarray, wherein the monodisperse polymer particles have a particle size distribution coefficient of less than 10%. In fact, as discussed above neither of these references teaches a coefficient of less than 20%. The Examiner relies on Waki to teach this.

It is respectfully urged that Waki is non-analogous art for the following reasons. In order to rely on a reference as a basis for rejection of Applicants' invention, a reference must either be in the field of the Applicants' endeavor or reasonably pertain to the particular problem with which the invention is concerned The cited reference is not in Applicants' field of endeavor, that is Waki relates to an optical recording medium such as those used in hard drives. The present invention as discussed above relates to a microarray having a support attached to a surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles. Waki fails to teach polymer particles with a mean diameter of 0.05 to 50 microns. In fact, Waki only discloses ultrafine metal particles (paragraph 0045). Furthermore, Waki teaches away from utilizing particles with a mean diameter of 0.05 to 50 microns, much less the use of polymer particles within the size limitation. The reference states that a size of more than 50 nm results in deterioration of recording characteristics (paragraph 0045). This is also evidence as to the differences in the problems solved by the two inventions. The present invention improves the immobilization capacity of biological microarrays. Whereas, Waki is concerned with optical recording medium that is high is sensitivity and excellent in information keeping quality,

and in no way mentions biological microarrays. Biological microarrays do not have the problem of recoding characteristic deterioration, as the microarrays are not intended for recording. Furthermore, the U.S. Patent and Trademark Office Classification is evidence of analogy. The references cited by the Examiner are contained in different classifications. Waki is classified in Class 369/172, Dynamic Information Storage or Retrieval by replacement, whereas Wohlstadter is classified in class 435/6, Chemistry: Molecular Biology and Microbiology involving nucleic acid, and Pierce is classified in class 422/56, Chemical Apparatus and Process Disinfecting, Deodorizing, Preserving, or Sterilizing have reagent in absorbent or bibulous substrate. The present invention makes no reference to optical information storage. Therefore, it is respectfully urged that Waki does not suggest combination with the other references. Furthermore, Waki is not concerned with the problem disclosed by the instant invention, and is therefore non-analogous art.

Alternatively, even if Waki is considered analogous art the reference fails to teach polymer particles within the range from 0.05 to 50 microns as claimed by the instant invention. As discussed above Waki only teaches the use of ultrafine metal particles not polymer particles (paragraph 0045). Furthermore, as discussed above Waki teaches away from the use of particles with sizes greater than 50 nm (paragraph 0045). Therefore, it is respectfully urged that the combination of these references would not lead one of ordinary skill in the art to the instant invention. Furthermore, claim 34 as originally filed does not stand rejected under these references, and is now incorporated into independent claim 1. Claim 7 benefits from dependency on claim 1, which as discussed above is patentable. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

Rejection of Claims 12, 27-30, 34 and 35 Under 35 U.S.C. §103(a):

The Examiner has rejected claims 12, 27-30, 34 and 35 under 35 U.S.C. §103(a) as being unpatentable over Wohlstadter et al. (U.S. Patent No. 6,066,448) in view of Snyder et al. (U.S. Patent No. 5,094,962).

The Examiner indicates that Wohlstadter et al. teaches a microarray as discussed above. The Examiner states that Wohlstadter et al. fails to teach a microarray, wherein the polymer particles comprise chemically active groups, which comprise vinylsulfonyl units and stabilizer polymers comprise at

least one member selected from the group consisting of acrylic acid and (meth)acrylic acid. The Examiner further states that Wohlstadter et al. fails to teach a microarray, wherein polymer particles comprise at least one ethylenically unsaturated polymerizable monomer.

The Examiner indicates that Snyder et al. teaches a method of preparing microporous substrate having a first and second outer surfaces and having affixed to at least one of the surfaces a composition comprising a specific binding reagent, which comprises water-insoluble particles to which are attached receptor molecules to the target ligand, the reagent admixed with one or more hydrophilic, neutral or positively-charged polymeric binders (column 2, lines 50-57). The Examiner indicates that the reagents are prepared using polymeric particles, which have suitable reactive groups for covalently attaching the receptor molecules thereto (column 6, lines 35-37). Covalent attachment of receptor is usually accomplished using surface reactive groups, which are capable of reacting directly or indirectly with free amine or vinylsuifonyl groups of the ligand (column 6, lines 45-49). Such surface reactive groups include vinylsulfonyl and other groups known in the art (column 6, lines 46-49). The Examiner states that Snyder teaches polymer particles having a mean diameter of from 0.01 to 5 microns.

The Examiner indicates that it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the microarray of Wohlstadter et al. with polymeric particles having vinylsulfonyl as a reactive group as taught by Snyder et al. in order to covalently attach the receptor molecules thereto for use in a ligand receptor assay to detect a target ligand. This rejection is respectfully traversed.

Wohlstadter discloses materials and methods for producing patterned multi- array, multi-specific surfaces that are electronically excited for use in electrochemiluminescence based tests. Materials and methods are provided for the chemical and/or physical control of conducting domains and reagent deposition for use in flat panel displays and multiply specific testing procedures.

Snyder relates to a microporous article comprising a stabilized specific binding reagent, and to its use in a method for detecting a target ligand. It also relates to a diagnostic test kit comprising the article. The invention is useful in diagnostic methods. Snyder discloses a water-insoluble microporous article

comprises a microporous substrate having first and second outer surfaces. Affixed to at least one of those surfaces is a stabilized specific binding reagent admixed with certain hydrophilic, neutral or positively-charged binder materials. Particularly useful binder materials include certain quaternary polymers, vinylpyrrolidone polymers and acrylamide polymers. In this mixture, the reagent exhibits improved keeping stability compared to similar reagents used without binder materials. The reagent comprises water-insoluble particles to which are attached receptor molecules to a target ligand. Substantially none of the reagent is entrapped within the microporous substrate. This article is useful for the detection of a target ligand in an assay involving the specific binding reaction of the ligand with corresponding receptor molecules, and can be included in a diagnostic test kit. It is particularly useful for the detection of Streptococcal antigen in a biological specimen when the receptor molecules are antibodies to that antigen.

The present invention relates to a microarray comprising a support having attached to a surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles, which have a particle size distribution coefficient of variation of less than 20% and a mean diameter of from 0.05 to 50 microns.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the references or in the general knowledge available to one skilled in the art to modify the references, there must be a reasonable expectation of success, and the prior art references must teach or suggest all the claim limitations. Original claim 1 has been amended to include previously dependent claims 5, 6, and 34. As noted by the Examiner Wohlstadter fails to teach monodisperse polymer particles. Snyder does not teach the importance of utilizing monodisperse polymer particles with a particle size distribution coefficient of less than 20%. Therefore, it is respectfully urged that Wohlstadter in view of Snyder fails to teach or suggest a microarray having monodisperse polymer particles with a particle size distribution coefficient of less than 20% as claimed in the instant invention. Furthermore, claims 5 and 6 as originally filed do not stand rejected under these references, and are now incorporated into independent claim 1. Claims 12, 27-30 and 35 benefit from dependency on claim

1, which as discussed above is patentable. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

Rejection of Claims 14 and 15 Under 35 U.S.C. §103(a):

The Examiner has rejected claims 14 and 15 under 35 U.S.C. §103(a) as being unpatentable over Wohlstadter et al. (U.S. Patent No. 6,066,448) in view of Pierce et al. (U.S. Patent No. 4,258,001) as applied to claim 13 above, and further in view of Snyder et al. (U.S. Patent No. 5,094,962).

The Examiner indicates that Wohlstadter et al. in view of Pierce et al. teaches a microarray comprising a stabilizer polymer as discussed above. The Examiner states that Pierce et al. teaches a stabilizer polymer comprising a monomer blend containing from monomers selected from groups (a)-(k) (column 14, lines 58-61) such as acrylamide (column 12, line 3) having a crosslinking vinylsulfonyl group (column 12, lines 36-42). The Examiner indicates that Wohlstadter et al. in view of Pierce et al. fails to teach a microarray, wherein stabilizer polymers comprise at least one member selected from group consisting of poly(propyleneimine), polymers and copolymers of methacrylic acid, acrylic acid, mercaptomethyl styrene, N-aminopropyl(meth)acrylamide and secondary amine derivatives thereof, N-aminoethyl(meth)acrylate and secondary amine forms thereof, diallyamine, vinylbenzylamine, vinylamine, (meth)acrylic acid, vinylbenzyl mercaptan, and hydroxyethyl(meth)acrylate.

The Examiner indicates that Snyder et al. teaches a method of preparing microporous substrate having a first and second outer surfaces and having affixed to at least one of the surfaces a composition comprising a specific binding reagent, which comprises water-insoluble particles to which are attached receptor molecules to the target ligand, the reagent admixed with one or more hydrophilic, neutral or positively-charged polymeric binders (column 2, lines 50-57). The Examiner states that the reagents are prepared using polymeric particles, which have suitable reactive groups for covalently attaching the receptor molecules thereto (column 6, lines 35-37). The binder material improves the keeping stability of the reagent considerably over the same reagent used without the binder material (column 4, lines 60-62).

The Examiner states that it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the microarray of Wohlstadter et al. in view of Pierce et al. with hydrophilic, neutral or positively

charged binder material admixed with reagent comprising polymer particles as taught by Snyder et al. in order to improve stability of reagent. This rejection is respectfully traversed.

Wohlstadter discloses materials and methods for producing patterned multi- array, multi-specific surfaces that are electronically excited for use in electrochemiluminescence based tests. Materials and methods are provided for the chemical and/or physical control of conducting domains and reagent deposition for use in flat panel displays and multiply specific testing procedures.

Pierce discloses an element for the analysis or transport of liquid, especially aqueous liquids, contains a structure comprising a plurality of heat-stable, organo-polymeric particles non-swellable in and impermeable to the liquid, and an adhesive concentrated at particle surface areas contiguous to adjacent particles bonding the particles into a coherent, three-dimensional lattice that is non-swellable in the liquid. A substantial portion of the particle surface area in this lattice structure is therefore effectively free from adhesive. The lattice structure has interconnected void spaces among the particles representing a total void volume of about 25 to 80 percent to provide for transport of the liquid. The adhesive comprises an organic polymer different from that of the particles and insoluble in the liquid under analysis. The amount of adhesive in the structure is less than 10 weight percent of the particles. The particulate structure of these elements can contain interactive compositions useful for the analysis of various substances in liquids, especially high molecular weight proteinaceous substances in aqueous biological liquids. Multi-zone elements containing, in fluid contact, at least two zones having a particulate structure as described above or one such zone together with other functional zones are also disclosed. These structures are particularly useful in the "dry chemistry" analysis of aqueous liquids. "Dry chemistry" analysis refers to analytical methods and techniques that are carried out using chemical reagents contained in various "dry-to-the-touch" test elements such as "dip-and-read" test strips, multilayer test elements and the like.

Snyder relates to a microporous article comprising a stabilized specific binding reagent, and to its use in a method for detecting a target ligand. It also relates to a diagnostic test kit comprising the article. The invention is useful in diagnostic methods. Snyder discloses a water-insoluble microporous article comprises a microporous substrate having first and second outer surfaces.

Affixed to at least one of those surfaces is a stabilized specific binding reagent admixed with certain hydrophilic, neutral or positively-charged binder materials. Particularly useful binder materials include certain quaternary polymers, vinylpyrrolidone polymers and acrylamide polymers. In this mixture, the reagent exhibits improved keeping stability compared to similar reagents used without binder materials. The reagent comprises water-insoluble particles to which are attached receptor molecules to a target ligand. Substantially none of the reagent is entrapped within the microporous substrate. This article is useful for the detection of a target ligand in an assay involving the specific binding reaction of the ligand with corresponding receptor molecules, and can be included in a diagnostic test kit. It is particularly useful for the detection of Streptococcal antigen in a biological specimen when the receptor molecules are antibodies to that antigen.

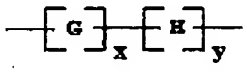
The present invention relates to a microarray comprising a support having attached to a surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles, which have a particle size distribution coefficient of variation of less than 20% and a mean diameter of from 0.05 to 50 microns.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the references or in the general knowledge available to one skilled in the art to modify the references, there must be a reasonable expectation of success, and the prior art references must teach or suggest all the claim limitations. Original claim 1 has been amended to include previously dependent claims 5, 6, and 34. As noted by the Examiner Wohlstadter fails to teach monodisperse polymer particles. As discussed above, Pierce fails to teach or suggest monodisperse polymer particles with a variation coefficient of less than 20%. As discussed above Wohlstadter, Pierce and Snyder fail to teach or suggest monodisperse polymer particles with the required coefficient of variation of less than 20% and a mean diameter of 0.05 to 50 microns as claimed in the instant invention as amended. Furthermore, claims 5, 6 and 34 as originally filed do not stand rejected under these references, and are now incorporated into independent claim 1. Claims 14 and 15 benefit from dependency on claim 1, which as discussed above is patentable. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

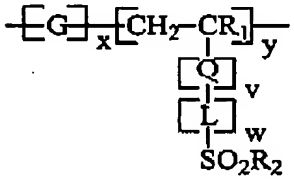
Rejection of Claims 25 and 26 Under 35 U.S.C. §103(a):

The Examiner has rejected claims 25 and 26 under 35 U.S.C. §103(a) as being unpatentable over Wohlstadter et al. (U.S. Patent No. 6,066,448) in view of Pierce et al. (U.S. Patent No. 4,258,001) as applied to claims 13, 16, and 17 above, and further in view of Ogawa et al. (U.S. Patent No. 4,548,869).

The Examiner indicates that Wohlstadter et al. in view of Pierce et al. teaches a microarray comprising a stabilizer polymer as discussed above. The Examiner states that Pierce et al. teaches a stabilizer polymer comprising a monomer blend containing from monomers selected from groups (a)-(k) (column 14, lines 58-61) such as acrylamide (column 12, line 3) having a crosslinking vinylsulfonyl group (column 12, lines 36-42). The Examiner states that Wohlstadter et al. in view of Pierce et al. fails to teach a microarray, wherein the vinylsulfone or vinylsulfone precursor "H" of Formula I represents groups represented by Formula II:

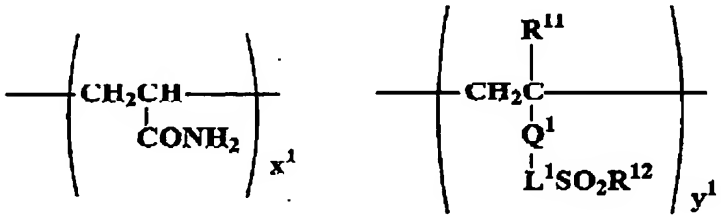


Formula I



Formula II

The Examiner indicates that Ogawa et al. teaches an adhesive layer to improve adhesion between a support and a polyacrylamide gel medium (column 2, lines 34-37) and the adhesive layer comprising a polymer having at least one specifically selected repeated unit having the following formula:



in which R^{11} is a hydrogen atom or an alkyl group containing 1-6 carbon atoms; Q^1 is -COO-, $CON(R^{11})$- or an arylene group containing 6-10 carbon atoms; L^1 is a divalent group containing at least one linkage selected from the group consisting of -COO- and $-CON(R^{11})$- and containing 3-15 carbon atoms, or divalent atom containing at least one linkage selected from the group consisting of -O-, $-N(R^{11})$ -, - CO-, -SO-, $-SO_2$-, $-SO_3$-, $-S0_2N(R^{11})$ -, $-N(R^{11})CON(R^{11})$ and $-N(R^{11})COO$-, and containing 1-12 carbon atoms, in which R^{11} has the same meaning as defined above; R^{12} is $-CH=CH_2$ or $-CH_2CH_2X^1$, in which X^1 is a substituent replaceable with a nucleophilic group or releasable in the form of HX^1 by a base and x^1 and y^1 both representing molar percentage rankle from 0 to 99 and from 1 to 100, respectively, and x^1+y^1 is not less than 90 (column 2 line 47-column 3, line 12). Ogawa et al. further teaches a process for synthesis of athylenic unsaturated monomers containing a vinylsulfonyl group or function group convertible into vinylsulfonyl group, which are employable for the preparation of polymers comprising repeating unit represented by the formula above.

The Examiner states that it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the stabilizer polymer composition of vinylsulfone or vinylsulfone precursor "H" of Formula I as taught by Wohlstadter et al. in view of Pierce et al. with an adhesive layer having the formula of Ogawa et al. in order to function as a stabilizer by improving adhesion between a support and a polyacrylamide gel medium. This rejection is respectfully traversed.

Wohlstadter discloses materials and methods for producing patterned multi- array, multi-specific surfaces that are electronically excited for use in electrochemiluminescence based tests. Materials and methods are provided for the chemical and/or physical control of conducting domains and reagent deposition for use in flat panel displays and multiply specific testing procedures.

Pierce discloses an element for the analysis or transport of liquid, especially aqueous liquids, contains a structure comprising a plurality of heat-stable, organo-polymeric particles non-swellable in and impermeable to the liquid, and an adhesive concentrated at particle surface areas contiguous to adjacent particles bonding the particles into a coherent, three-dimensional lattice that is non-swellable in the liquid. A substantial portion of the particle surface

area in this lattice structure is therefore effectively free from adhesive. The lattice structure has interconnected void spaces among the particles representing a total void volume of about 25 to 80 percent to provide for transport of the liquid. The adhesive comprises an organic polymer different from that of the particles and insoluble in the liquid under analysis. The amount of adhesive in the structure is less than 10 weight percent of the particles. The particulate structure of these elements can contain interactive compositions useful for the analysis of various substances in liquids, especially high molecular weight proteinaceous substances in aqueous biological liquids. Multi-zone elements containing, in fluid contact, at least two zones having a particulate structure as described above or one such zone together with other functional zones are also disclosed. These structures are particularly useful in the "dry chemistry" analysis of aqueous liquids. "Dry chemistry" analysis refers to analytical methods and techniques that are carried out using chemical reagents contained in various "dry-to-the-touch" test elements such as "dip-and-read" test strips, multilayer test elements and the like.

Ogawa relates to an element for electrophoresis, especially to an element for electrophoresis suitably employable for determination of base sequence of DNA, RNA, their fragment, and their derivatives, by disclosing an element for electrophoresis comprising the following three-layer structure laminated in the order: (I) a support layer; (II) an adhesive layer comprising a polymer having at least one specifically selected repeating unit; and (III) a medium layer for electrophoresis comprising an aqueous polyacrylamide gel formed by crosslinking polymerization of an acrylamide compound and a crosslinking agent in the presence of water, and a compound containing at least one carbamoyl group (modifier).

The present invention relates to a microarray comprising a support having attached to a surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles, which have a particle size distribution coefficient of variation of less than 20% and a mean diameter of from 0.05 to 50 microns.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the references or in the general knowledge available to one skilled in the art to modify the references, there must be a reasonable expectation of success, and the prior art references must teach or suggest all the

claim limitations. Original claim 1 has been amended to include previously dependent claims 5, 6, and 34. As noted by the Examiner Wohlstadter fails to teach monodisperse polymer particles. As discussed above, Pierce fails to teach or suggest monodisperse polymer particles with a variation coefficient of less than 20%. As discussed above Wohlstadter and Pierce fail to teach or suggest monodisperse polymer particles with the required coefficient of variation of less than 20% and a mean diameter of 0.05 to 50 microns as claimed in the instant invention as amended. As noted by the Examiner neither Wohlstadter nor Pierce teaches a microarray, wherein the monodisperse polymer particles have a particle size distribution coefficient of less than 10%. In fact, as discussed above neither of these references teaches a coefficient of less than 20%. In addition Ogawa fails to teach or suggest a microarray with monodisperse polymer particles have a particle size distribution coefficient of less than 20%. Therefore, it is respectfully urged that no reference alone or in combination teaches or suggests all of the instant invention's claimed limitations. Furthermore, claims 5, 6 and 34 as originally filed do not stand rejected under these references, and are now incorporated into independent claim 1. Claims 25 and 26 benefit from dependency on claim 1, which as discussed above is patentable. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

Rejection of Claims 27 and 31 Under 35 U.S.C. §103(a):

The Examiner has rejected claims 27 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wohlstadter et al. (U.S. Patent No. 6,066,448) in view of Molteberg et al. (U.S. Patent No. 6,787,233).

The Examiner indicates that Wohlstadter et al. teaches a microarray as discussed above. The Examiner states that Wohlstadter et al. fails to teach a microarray, wherein the polymer particles comprise monodisperse polymer particles.

The Examiner indicates that Molteberg et al. teaches a method of preparing monodisperse polymer particles comprising trimethylolpropane (column 2, line 62). The particles of Molteberg et al. may be used for purposes in medical diagnostic assay and gene therapy (column 5, lines 63-64).

The Examiner states that it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the microarray of Wohlstadter et al. with the polymer particles comprising trimethylolpropane of

Molteberg et al. in order to use in applications such as medical diagnostic assay and gene therapy. This rejection is respectfully traversed.

Wohlstadter discloses materials and methods for producing patterned multi- array, multi-specific surfaces that are electronically excited for use in electrochemiluminescence based tests. Materials and methods are provided for the chemical and/or physical control of conducting domains and reagent deposition for use in flat panel displays and multiply specific testing procedures.

Molteberg relates to electroconductive particles, in particular gold-coated polymer microbeads, and to a process for their preparation. Particularly, Molteberg provides electroconductive particles comprising a styrene copolymer core and an external gold coating, characterised in that as said copolymer core is used a styrene copolymer comprising less than 50 wt. % styrene residues.

The present invention relates to a microarray comprising a support having attached to a surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles, which have a particle size distribution coefficient of variation of less than 20% and a mean diameter of from 0.05 to 50 microns.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the references or in the general knowledge available to one skilled in the art to modify the references, there must be a reasonable expectation of success, and the prior art references must teach or suggest all the claim limitations. Original claim 1 has been amended to include previously dependent claims 5, 6, and 34. As noted by the Examiner Wohlstadter fails to teach monodisperse polymer particles.

It is respectfully urged that Molteberg is non-analogous art for the following reasons. In order to rely on a reference as a basis for rejection of Applicants' invention, a reference must either be in the field of the Applicants' endeavor or reasonably pertain to the particular problem with which the invention is concerned. The cited reference is not in Applicants' field of endeavor, that is Molteberg relates to electroconductive particles with a styrene copolymer core and an external metal coating. The present invention as discussed above relates to a microarray having a support having attached to surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles. Molteberg fails to disclose a microarray having a support with at least on porous

layer containing a hydrophilic binder and monodisperse polymer particles. Molteberg mentions the use of gold-plated palladinated particles for uses other than the preferred use of providing electrical connections. The reference discloses that the gold-plated particles may be used in almost any of the currently existing uses for gold and gold plated microbeads. The present invention improves the immobilization capacity of biological microarrays, which is not a currently existing use for gold or gold-plated microbeads. Molteberg improves the quality of gold-plated styrene microspheres and does not suggest improved immobilization capacity of biological microarrays as disclosed in the instant invention. Molteberg fails to disclose a support or a hydrophilic binder. Molteberg only mentions metal-plated particles and does not disclose the monodisperse polymer particles as disclosed in the instant invention. Furthermore, the U.S. Patent and Trademark Office Classification is evidence of analogy. The references cited by the Examiner are contained in different classifications. Molteberg is classified in Class 428/403, Coated Particulate Matter Stock Material or Miscellaneous Articles, whereas Wohlstadter is classified in class 435/6, Chemistry: Molecular Biology and Microbiology involving nucleic acid. Therefore, it is respectfully urged that Molteberg does not suggest combination with the other reference. Furthermore, Molteberg is not concerned with the problem disclosed by the instant invention, and is therefore non-analogous art.

Furthermore, claims 5, 6 and 34 as originally filed do not stand rejected under these references, and are now incorporated into independent claim 1. Claims 27 and 31 benefit from dependency on claim 1, which as discussed above is patentable. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

Rejection of Claims 32 and 33 Under 35 U.S.C. §103(a):

The Examiner has rejected claims 32 and 33 under 35 U.S.C. 103(a) as being unpatentable over Wohlstadter et al. (U.S. Patent No. 6,066,448) in view of Snyder et al. (U.S. Patent No. 5,094,962) as applied to claim 27 above, and further in view of Frechet et al. (U.S. Patent No. 5,306,561).

The Examiner indicates that Wohlstadter et al. in view of Snyder et al. teaches a microarray as discussed above. The Examiner states that Wohlstadter in view of Snyder et al. fails to teach a microarray, wherein the

polymer particles comprise at least one or more water-soluble ethylenically unsaturated monomers, which includes acrylic and methacrylic acids.

The Examiner indicates that Frechet et al. teaches a method of producing polymer particles having a hydrophobic core and various surface functional groups, particularly hydrophilic and chiral surface functional groups (Abstract) resulting in polymer particles comprising water-soluble monomers such as acrylic and methacrylic acids (column 4, lines 54-68). The polymer particles (beads) are particularly useful in a variety of applications including enzyme immobilization (column 3, lines 44-50).

The Examiner states that it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the microarray of Wohlstadter et al. in view of Snyder et al. with polymer particles comprising water-soluble ethylenically unsaturated monomers such as acrylic and methacrylic acids as taught by Frechet et al. in order to use in applications such as enzyme immobilization. This rejection is respectfully traversed.

Wohlstadter discloses materials and methods for producing patterned multi array, multi-specific surfaces that are electronically excited for use in electrochemiluminescence based tests. Materials and methods are provided for the chemical and/or physical control of conducting domains and reagent deposition for use in flat panel displays and multiply specific testing procedures.

Snyder relates to a microporous article comprising a stabilized specific binding reagent, and to its use in a method for detecting a target ligand. It also relates to a diagnostic test kit comprising the article. The invention is useful in diagnostic methods. Snyder discloses a water-insoluble microporous article comprises a microporous substrate having first and second outer surfaces. Affixed to at least one of those surfaces is a stabilized specific binding reagent admixed with certain hydrophilic, neutral or positively-charged binder materials. Particularly useful binder materials include certain quaternary polymers, vinylpyrrolidone polymers and acrylamide polymers. In this mixture, the reagent exhibits improved keeping stability compared to similar reagents used without binder materials. The reagent comprises water-insoluble particles to which are attached receptor molecules to a target ligand. Substantially none of the reagent is entrapped within the microporous substrate. This article is useful for the detection of a target ligand in an assay involving the specific binding reaction of

the ligand with corresponding receptor molecules, and can be included in a diagnostic test kit. It is particularly useful for the detection of Streptococcal antigen in a biological specimen when the receptor molecules are antibodies to that antigen.

Frechet discloses polymer particles having a hydrophobic core and various surface functional groups, particularly hydrophilic and chiral surface functional groups, are produced by adding a non-emulsified functional polymerizable monomer to the aqueous phase of a dispersion of soluble polymer particles that have previously been swollen with an emulsified-monomer and polymerizing the monomers. Preferably the particles are uniform macroporous beads.

The present invention relates to a microarray comprising a support having attached to a surface thereof at least one porous layer containing a hydrophilic binder and monodisperse polymer particles, which have a particle size distribution coefficient of variation of less than 20% and a mean diameter of from 0.05 to 50 microns.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the references or in the general knowledge available to one skilled in the art to modify the references, there must be a reasonable expectation of success, and the prior art references must teach or suggest all the claim limitations. Original claim 1 has been amended to include previously dependent claims 5, 6, and 34. As noted by the Examiner Wohlstadter fails to teach monodisperse polymer particles. As discussed above Wohlstadter and Snyder fail to teach or suggest monodisperse polymer particles with the required coefficient of variation of less than 20% and a mean diameter of 0.05 to 50 microns as claimed in the instant invention as amended. Frechet does not teach monodisperse polymer particles with a particle size distribution coefficient of less than 20%, much less for use in a biological microarray. Therefore, it is respectfully urged that Wohlstadter in view of Snyder and further in view of Frechet does not teach or suggest monodisperse polymer particles with the required coefficient of variation of less than 20% and a mean diameter of 0.05 to 50 microns as claimed in the present invention. Furthermore, claims 5, 6 and 34 as originally filed do not stand rejected under these references, and are now incorporated into independent claim 1. Claims 32 and 33 benefit from

dependency on claim 1, which as discussed above is patentable. Therefore, it is respectfully requested that this rejection be reconsidered and withdrawn.

Provisional Double Patenting Rejections:

The Examiner has provisionally rejected claims 1-4, 8-12, 12-15, 27-30, 34-37, 43, 51 and 52 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27, 28, and 29-33 of copending Application No. 09/942,241 in view of Snyder et al. (U.S. Patent No. 5,094,962). Independent claim 1 now includes all of the limitations of claims 5 and 6, which do not stand rejected under Application No. 09/942,241 in view of Snyder et al. Therefore, it is respectfully requested that this provisional rejection is now moot and that the rejection be withdrawn.

The Examiner has provisionally rejected claims 1-4, 8-12, 12-15, 27-30, 34-37, 43, 51 and 52 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-16 of copending Application No. 10/062,326 in view of Snyder et al. (U.S. Patent No. 5,094,962). Independent claim 1 now includes all of the limitations of claims 5 and 6, which do not stand rejected under Application No. 10/062,326 in view of Snyder et al. Therefore, it is respectfully requested that this provisional rejection is now moot and that the rejection be withdrawn.

The Examiner has provisionally rejected claims 1-4, 8-12, 12-15, 27-30, 34-36, 43, 51, and 52 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/625,424 in view of Snyder et al. (U.S. Patent No. 5,094,962). Independent claim 1 now includes all of the limitations of claims 5 and 6, which do not stand rejected under Application No. 10/625,424 in view of Snyder et al. Therefore, it is respectfully requested that this provisional rejection is now moot and that the rejection be withdrawn.

The Examiner has provisionally rejected claims 1-4, 8-12, 12-15, 27-30, 34-37, 43, 51, and 52 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-16 of copending Application No. 10/625,637 in view of Snyder et al. (U.S. Patent No. 5,094,962). Independent claim 1 now includes all of the limitations of claims 5 and 6, which do not stand rejected under Application No. 10/625,637 in view of Snyder et al.

Therefore, it is respectfully requested that this provisional rejection is now moot and that the rejection be withdrawn.

The Examiner has provisionally rejected claims 1-53 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 64 of copending Application No. 10/658,009 in view of Wohlstadter et al. (U.S. Patent No. 6,066,448). In accordance with 37 CFR 1.321(c) enclosed is a Terminal Disclaimer which is believed to overcome this provisional rejection. It is respectfully requested that this rejection be reconsidered and withdrawn in light of the Terminal Disclaimer filed over Application No. 10/658,009.

The Examiner has provisionally rejected claims 1-53 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-65 of copending Application No. 10/682,271 in view of Snyder et al. (U.S. Patent No. 5,094,962). In accordance with 37 CFR 1.321(c) enclosed is a Terminal Disclaimer which is believed to overcome this provisional rejection. It is respectfully requested that this rejection be reconsidered and withdrawn in light of the Terminal Disclaimer filed over Application No. 10/682,271.

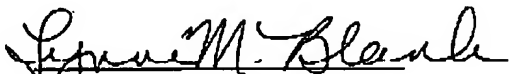
The Examiner has provisionally rejected claims 1-4, 8-12, 12-15, 27-30, 34-37, 43, 51, and 52 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 10/713,165 in view of Snyder et al. (U.S. Patent No. 5,094,962). Independent claim 1 now includes all of the limitations of claims 5 and 6, which do not stand rejected under Application No. 10/713,165 in view of Snyder et al. Therefore, it is respectfully requested that this provisional rejection is now moot and that the rejection be withdrawn.

The Examiner has provisionally rejected claims 1-4, 8-12, 12-15, 27-30, 34-37, 43, 51, and 52 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 10/713,246 in view of Snyder et al. (U.S. Patent No. 5,094,962). Independent claim 1 now includes all of the limitations of claims 5 and 6, which do not stand rejected under Application No. 10/713,246 in view of Snyder et al. Therefore, it is respectfully requested that this provisional rejection is now moot and that the rejection be withdrawn.

The Examiner has provisionally rejected claims 1-4, 8-12, 12-15, 27-30, 34-37, 43, 51, and 52 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 10/713,522 in view of Snyder et al. (U.S. Patent No. 5,094,962). Independent claim 1 now includes all of the limitations of claims 5 and 6, which do not stand rejected under Application No. 10/713,522 in view of Snyder et al. Therefore, it is respectfully requested that this provisional rejection is now moot and that the rejection be withdrawn.

It is believed that the foregoing is a complete response to the Office Action and that the claims are in condition for allowance. Favorable reconsideration and early passage to issue is therefore earnestly solicited.

Respectfully submitted,



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